

RECEIVED  
CENTRAL FAX CENTER

JAN 27 2006

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Diwu *et al.*

Serial No.: 10/713,670

Filed: November 13, 2003

For: **DERIVATIVES OF 1,2-DIHYDRO-7-HYDROXYQUINOLINES CONTAINING FUSED RINGS**

) Examiner: Fiona Powers

) Group Art Unit: 1626

) Docket No. MP0067.1 CIP

) **MARKED-UP VERSION OF THE CLAIMS**

Commissioner for Patents  
U.S. Patent and Trademark Office  
PO Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

The following Marked-up Version of the Claims is hereby submitted together with the Response to Office Action on or before the three (3) month due date of February 7, 2006.

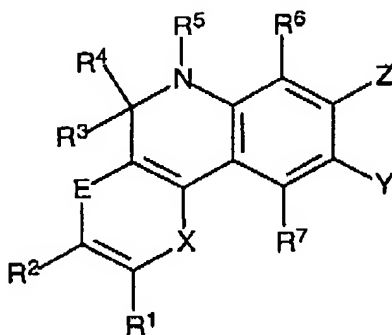
## CERTIFICATE OF TRANSMISSION

I HEREBY CERTIFY THAT THIS PAPER AND THE DOCUMENTS REFERRED AS BEING ATTACHED OR ENCLOSED HERewith ARE BEING FACSIMILE TRANSMITTED TO THE UNITED STATES PATENT AND TRADEMARK OFFICE ON 1/27-06 TO 1.571.273.8300  
By [Signature]

Diwu *et al.*  
Serial No. 10/713,670

We claim

1. (Currently Amended) A compound having a formula



wherein

R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, aryl, heteroaryl, -L-R<sub>x</sub> and -L-S<sub>c</sub>, wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

or R<sup>1</sup> in combination with R<sup>2</sup> forms a fused aromatic or heteroaromatic ring that is optionally sulfonated one or more times, or said ring is substituted by -L-R<sub>x</sub> or -L-S<sub>c</sub>;

or R<sup>2</sup> in combination with R<sup>3</sup> forms a 5- or 6-membered alicyclic ring;

R<sup>3</sup> and R<sup>4</sup> are independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, aromatic or heteroaromatic ring, -L-R<sub>x</sub> and -L-S<sub>c</sub>, wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, hydroxy, or halogen and said aromatic or heteroaromatic ring is optionally substituted one or more times by C<sub>1</sub>-C<sub>6</sub>

Diwu *et al.*

Serial No. 10/713,670

alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, C<sub>1</sub>-C<sub>6</sub> perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or R<sup>3</sup> in combination with R<sup>4</sup> forms a 5- or 6-membered alicyclic ring;

R<sup>5</sup> is independently selected from the group consisting of hydrogen, methyl, carboxymethyl, C<sub>2</sub>-C<sub>6</sub> alkyl, aryl, heteroaryl, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen and said aryl or heteroaryl is optionally substituted one or more times by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

R<sup>6</sup> is independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, aryl, heteroaryl, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

or R<sup>4</sup> in combination with R<sup>5</sup>, or R<sup>5</sup> in combination with R<sup>6</sup>, forms a 5- or 6-membered alicyclic ring;

R<sup>7</sup> is independently selected from the group consisting of hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, -L-R<sub>x</sub> and -L-S<sub>C</sub>;

one of X and E is O, S, or NR<sup>8</sup>, or  $\text{CR}^{\text{A}}=\text{CR}^{\text{B}}$ , and the other is absent;

wherein R<sup>8</sup> is independently selected from the group consisting of hydrogen, methyl, carboxymethyl, C<sub>2</sub>-C<sub>6</sub> alkyl, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; and

R<sup>1</sup> and R<sup>2</sup> are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid, C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> alkoxy, aryl, heteroaryl, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl or alkoxy is optionally substituted by carboxylic acid,

Diwu *et al.*  
Serial No. 10/713,670

sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by C<sub>1</sub>-C<sub>6</sub> alkyl, C<sub>1</sub>-C<sub>6</sub> perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

Y is independently selected from the group consisting of H, OH, NH<sub>2</sub>, NO, -(CO)-R<sup>9</sup>, -(CO)-O-R<sup>10</sup>, wherein said R<sup>9</sup> and R<sup>10</sup> are independently H, C<sub>1</sub>-C<sub>6</sub> alkyl, or a substituted or unsubstituted aryl or heteroaryl ring system having 1-2 rings;

Z is independently selected from the group consisting of H, OH, NHR<sup>17</sup>, SH, or C(CR<sup>11</sup>R<sup>12</sup>)<sub>2</sub>OH; wherein said R<sup>17</sup> is a C<sub>1</sub>-C<sub>6</sub> alkyl that is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen and said R<sup>11</sup> and R<sup>12</sup> are independently C<sub>1</sub>-C<sub>6</sub> alkyl that are optionally substituted by carboxylic acid, sulfonic acid, or halogen, or R<sup>11</sup> and R<sup>12</sup> taken in combination form a 5- or 6-membered alicyclic ring;

wherein L is a covalent linkage;

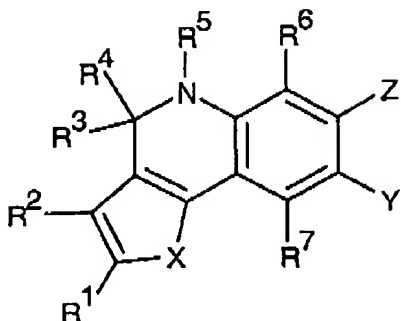
R<sub>x</sub> is a reactive group; and

S<sub>c</sub> is a conjugated substance;

with the proviso that when R<sup>1</sup> and R<sup>2</sup> form a fused aromatic ring, R<sup>8</sup> is not hydrogen or a C<sub>2</sub> alkyl substituted by carboxylic acid.

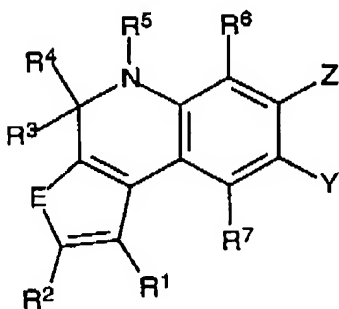
2. (Currently Amended) The compound according to Claim 1, wherein one of X and E is O, or S, or ~~CR<sup>1</sup>=CR<sup>2</sup>~~, and the other is absent.
3. (Original) The compound according to Claim 2, wherein said compound has the formula

Diwu *et al.*  
Serial No. 10/713,670



wherein X is O or S.

4. (Original) The compound according to Claim 2, wherein said compound has the formula



wherein E is O or S.

5. (Original) The compound according to Claim 3, wherein X is S.
6. (Original) The compound according to Claim 1, wherein

R<sup>1</sup> is hydrogen or sulfonic acid;

R<sup>3</sup> and R<sup>4</sup> are each methyl;

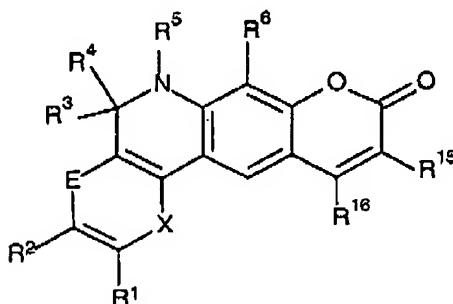
R<sup>6</sup> and R<sup>7</sup> are each hydrogen or methyl; and

Diwu *et al.*

Serial No. 10/713,670

Z is OH.

7. (Original) The compound according to Claim 1, wherein Y is H or -(CO)-H or NO.
8. (Original) The compound according to Claim 1, wherein said L is independently a single covalent bond or a covalent linkage having 1-20 nonhydrogen atoms selected from the group consisting of C, N, O, P, and S.
9. (Original) The compound according to Claim 1, wherein said R<sub>x</sub> is independently selected from the group consisting of an acrylamide, an activated ester of a carboxylic acid, an acyl azide, an acyl nitrile, an aldehyde, an alkyl halide, an amine, an anhydride, an aniline, an aryl halide, an azide, an aziridine, a boronate, a carboxylic acid, a diazoalkane, a haloacetamide, a halotriazine, a hydrazine, an imido ester, an isocyanate, an isothiocyanate, a maleimide, a phosphoramidite, a reactive platinum complex, a sulfonyl halide, and a thiol group.
10. (Original) The compound according to Claim 1, wherein said S<sub>C</sub> is independently selected from the group consisting of an amino acid, a peptide, a protein, a tyramine, a carbohydrate, an metal chelating moiety, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a hapten, a psoralen, a drug, a hormone, a lipid, a lipid assembly, a polymer, a polymeric microparticle, a biological cell, and a virus.
11. (Original) A compound having a formula



Diwu *et al.*  
Serial No. 10/713,670

wherein  $R^1$ ,  $R^2$ , and  $R^6$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^1$  in combination with  $R^2$  forms a fused aromatic or heteroaromatic ring that is optionally sulfonated one or more times, or said ring is substituted by  $-L-R_x$  or  $-L-S_c$ ;

$R^3$  and  $R^4$  are independently selected from the group consisting of hydrogen,  $C_1$ - $C_6$  alkyl, an aromatic or heteroaromatic ring,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, hydroxy, or halogen and said aromatic or heteroaromatic ring is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^2$  in combination with  $R^3$ , or  $R^3$  in combination with  $R^4$ , forms a 5- or 6-membered alicyclic ring;

$R^5$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2$ - $C_6$  alkyl, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^4$  in combination with  $R^5$ , or  $R^5$  in combination with  $R^6$ , forms a 5- or 6-membered alicyclic ring;

one of X and E is O, S,  $NR^8$ , or  $CR^{1'}=CR^{2'}$  and the other is absent;

Diwu *et al.*  
Serial No. 10/713,670

wherein  $R^6$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2-C_6$  alkyl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; and

$R^{1'}$  and  $R^{2'}$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid,  $C_1-C_6$  alkyl,  $C_1-C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

$R^{15}$  and  $R^{16}$  are independently selected from the group consisting of hydrogen, cyano, nitro, halogen, carboxylic acid, sulfonic acid,  $C_1-C_6$  alkyl, an aromatic or heteroaromatic ring system having 1-2 fused rings,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aromatic or heteroaromatic ring system is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

wherein L is a covalent linkage;

$R_x$  is a reactive group; and

$S_c$  is a conjugated substance.

12. (Original) The compound according to Claim 11, wherein said one of X and E is O or S.
13. (Original) The compound according to Claim 12, wherein

$R^6$  and  $R^7$  are hydrogen;

$R^3$  and  $R^4$  are each methyl;

$R^1$  is hydrogen or sulfonic acid;



Diwu *et al.*  
Serial No. 10/713,670

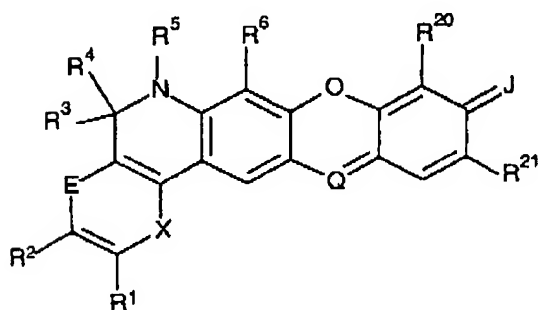
one of  $R^{15}$  and  $R^{16}$  is  $-L-R_x$  or  $-L-S_c$ , and the other is hydrogen,  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl; or cyano;

wherein L is a single covalent bond, or L is a covalent linkage having 1-20 nonhydrogen atoms selected from the group consisting of C, N, O, P, and S, and

wherein  $R_x$  is independently selected from the group consisting of an acrylamide, an activated ester of a carboxylic acid, an acyl azide, an acyl nitrile, an aldehyde, an alkyl halide, an amine, an anhydride, an aniline, an aryl halide, an azide, an aziridine, a boronate, a carboxylic acid, a diazoalkane, a haloacetamide, a halotriazine, a hydrazine, an imido ester, an isocyanate, an isothiocyanate, a maleimide, a phosphoramidite, a reactive platinum complex, a sulfonyl halide, and a thiol group; and

wherein  $S_c$  is independently selected from the group consisting of an amino acid, a peptide, a protein, a tyramine, a carbohydrate, a metal chelating moiety, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a hapten, a psoralen, a drug, a hormone, a lipid, a lipid assembly, a polymer, a polymeric microparticle, a biological cell, and a virus.

14. (Original) The compound according to Claim 11, wherein one of said  $R^{15}$  or  $R^{16}$  is an aromatic or heteroaromatic ring system having 1-2 fused rings that is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl.
15. (Original) A compound having a formula:



Diwu *et al.*  
Serial No. 10/713,670

wherein  $R^1$ ,  $R^2$ , and  $R^6$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_C$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^1$  in combination with  $R^2$  forms a fused aromatic or heteroaromatic ring that is optionally sulfonated one or more times, or said ring is substituted by  $-L-R_x$  or  $-L-S_C$ ;

$R^3$  and  $R^4$  are independently selected from the group consisting of hydrogen,  $C_1$ - $C_6$  alkyl, an aromatic or heteroaromatic ring,  $-L-R_x$  and  $-L-S_C$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, hydroxy, or halogen and said aromatic or heteroaromatic ring is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^2$  in combination with  $R^3$ , or  $R^3$  in combination with  $R^4$ , forms a 5- or 6-membered alicyclic ring;

$R^5$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2$ - $C_6$  alkyl, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_C$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^4$  in combination with  $R^5$ , or  $R^5$  in combination with  $R^6$ , forms a 5- or 6-membered alicyclic ring;

one of X and E is O, S,  $NR^8$ , or  $CR^{1'}=CR^{2'}$ , and the other is absent;

Diwu *et al.*  
Serial No. 10/713,670

wherein  $R^8$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2-C_6$  alkyl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; and

$R^{1'}$  and  $R^{2'}$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid,  $C_1-C_6$  alkyl,  $C_1-C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

$R^{20}$  and  $R^{21}$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid,  $C_1-C_6$  alkyl,  $C_1-C_6$  alkoxy, aromatic or heteroaromatic ring,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen said aromatic or heteroaromatic ring is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

J is O or  $NR^{37}R^{38}$ ;

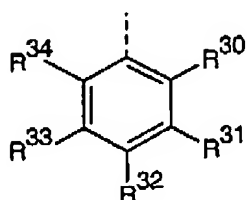
wherein  $R^{37}$  and  $R^{38}$  are independently selected from the group consisting of hydrogen,  $C_1-C_6$  alkyl, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; or  $R^{37}$  in combination with  $R^{38}$  forms a saturated 5- or 6-membered heterocycle that is a piperidine, a morpholine, a pyrrolidine or a piperazine, wherein said heterocycle is optionally substituted by methyl, carboxylic acid, or a carboxylic acid ester of a  $C_1-C_6$  alkyl;

or  $R^{37}$  in combination with  $R^{20}$ , or  $R^{38}$  in combination with  $R^{21}$ , or both, form a 5- or 6-membered ring that is saturated or unsaturated, and is optionally substituted by one or more sulfonic acids, or  $C_1-C_6$  alkyl that is optionally substituted by sulfonic acid;

Q is N or  $CR^{28}$ , wherein  $R^{28}$  is independently selected from the group consisting of hydrogen, F, CN, carboxylic acid, a carboxylic acid ester of a  $C_1-C_6$  alcohol, a  $C_1-C_6$

Diwu *et al.*  
Serial No. 10/713,670

alkyl, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; or R<sup>28</sup> comprises a formula



wherein R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> are independently selected from the group consisting of hydrogen, F, Cl, Br, I, sulfonic acid, carboxylic acid, CN, nitro, hydroxy, azido, amino, hydrazino, C<sub>1</sub>-C<sub>18</sub> alkyl, C<sub>1</sub>-C<sub>18</sub> alkoxy, C<sub>1</sub>-C<sub>18</sub> alkylthio, C<sub>1</sub>-C<sub>18</sub> alkanoylamino, C<sub>1</sub>-C<sub>18</sub> alkylaminocarbonyl, C<sub>2</sub>-C<sub>36</sub> dialkylaminocarbonyl, C<sub>1</sub>-C<sub>18</sub> alkyloxycarbonyl, C<sub>7</sub>-C<sub>18</sub> arylcarboxamido, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl or aryl portions of said R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> are optionally substituted one or more times by substituents selected from the group consisting of F, Cl, Br, I, hydroxy, carboxylic acid, a carboxylic acid ester of a C<sub>1</sub>-C<sub>6</sub> alcohol, sulfonic acid, amino, C<sub>1</sub>-C<sub>6</sub> alkylamino, C<sub>2</sub>-C<sub>6</sub> dialkylamino and C<sub>1</sub>-C<sub>6</sub> alkoxy; or a pair of adjacent R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> substituents when taken in combination, form a fused 6-membered aromatic ring that is optionally further substituted by carboxylic acid; and

wherein L is a covalent linkage;

R<sub>x</sub> is a reactive group; and

S<sub>C</sub> is a conjugated substance.

16. (Original) The compound according to Claim 15, wherein said Q is N.
17. (Original) The compound according to Claim 15, wherein said J is O and said Q is CR<sup>28</sup>.
18. (Original) The compound according to Claim 17, wherein one of said R<sup>5</sup>, R<sup>21</sup>, R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup>, and R<sup>34</sup> is -L-R<sub>x</sub> or -L-S<sub>C</sub>.

Diwu *et al.*  
Serial No. 10/713,670

19. (Original) The compound according to Claim 15, wherein

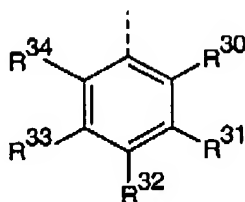
said  $R^3$  and  $R^4$  are each methyl;

$R^1$  is H or a sulfonic acid;

$R^6$  is H; and

J is  $NR^{37}R^{38}$ .

20. (Original) The compound according to Claim 19, wherein Q is  $CR^{28}$  and  $R^{28}$  has the formula



wherein one of  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$ , and  $R^{34}$  is  $-L-R_x$  or  $-L-S_c$ ; and

wherein L is a single covalent bond, or L is a covalent linkage having 1-20 nonhydrogen atoms selected from the group consisting of C, N, O, P, and S, and

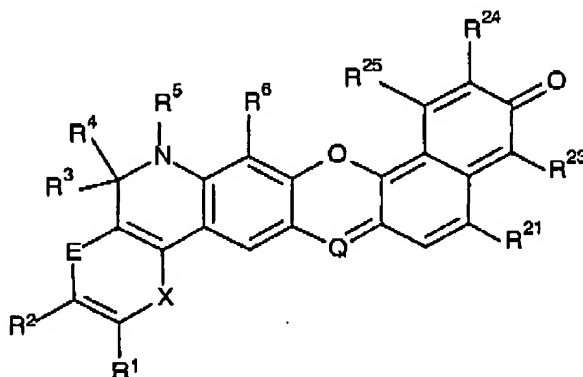
wherein  $R_x$  is independently selected from the group consisting of an acrylamide, an activated ester of a carboxylic acid, an acyl azide, an acyl nitrile, an aldehyde, an alkyl halide, an amine, an anhydride, an aniline, an aryl halide, an azide, an aziridine, a boronate, a carboxylic acid, a diazoalkane, a haloacetamide, a halotriazine, a hydrazine, an imido ester, an isocyanate, an isothiocyanate, a maleimide, a phosphoramidite, a reactive platinum complex, a sulfonyl halide, and a thiol group; and

wherein  $S_c$  is independently selected from the group consisting of an amino acid, a peptide, a protein, a tyramine, a carbohydrate, a metal chelating moiety, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a hapten, a psoralen, a drug, a hormone,

Diwu *et al.*  
Serial No. 10/713,670

a lipid, a lipid assembly, a polymer, a polymeric microparticle, a biological cell, and a virus.

21. (Original) A compound comprising a formula



wherein  $R^1$ ,  $R^2$ , and  $R^6$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^1$  in combination with  $R^2$  forms a fused aromatic or heteroaromatic ring that is optionally sulfonated one or more times, or said ring is substituted by  $-L-R_x$  or  $-L-S_c$ ;

$R^3$  and  $R^4$  are independently selected from the group consisting of hydrogen,  $C_1$ - $C_6$  alkyl, an aromatic or heteroaromatic ring,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, hydroxy, or halogen and said aromatic or heteroaromatic ring is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

Diwu *et al.*  
Serial No. 10/713,670

or  $R^2$  in combination with  $R^3$ , or  $R^3$  in combination with  $R^4$ , forms a 5- or 6-membered alicyclic ring;

$R^5$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2-C_6$  alkyl, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^4$  in combination with  $R^5$ , or  $R^5$  in combination with  $R^6$ , forms a 5- or 6-membered alicyclic ring;

one of E and X is O, S,  $NR^8$ , or  $CR^{1'}=CR^{2'}$ , and the other is absent;

wherein  $R^8$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2-C_6$  alkyl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; and

$R^{1'}$  and  $R^{2'}$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid,  $C_1-C_6$  alkyl,  $C_1-C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

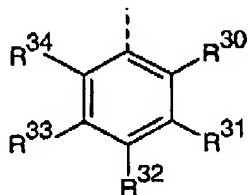
$R^{21}$ ,  $R^{23}$ ,  $R^{24}$ , and  $R^{25}$  are independently selected from the group consisting of hydrogen, cyano, nitro, halogen, carboxylic acid, sulfonic acid,  $C_1-C_6$  alkyl, aromatic or heteroaromatic ring,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, or halogen said aromatic or heteroaromatic ring is optionally substituted one or more times by  $C_1-C_6$  alkyl,  $C_1-C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

Q is N or  $CR^{28}$ , wherein  $R^{28}$  is independently selected from the group consisting of

Diwu *et al.*

Serial No. 10/713,670

hydrogen, F, CN, carboxylic acid, a carboxylic acid ester of a C<sub>1</sub>-C<sub>6</sub> alcohol, a C<sub>1</sub>-C<sub>6</sub> alkyl, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; or R<sup>28</sup> comprises a formula



wherein R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> are independently selected from the group consisting of hydrogen, F, Cl, Br, I, sulfonic acid, carboxylic acid, CN, nitro, hydroxy, azido, amino, hydrazino, C<sub>1</sub>-C<sub>18</sub> alkyl, C<sub>1</sub>-C<sub>18</sub> alkoxy, C<sub>1</sub>-C<sub>18</sub> alkylthio, C<sub>1</sub>-C<sub>18</sub> alkanoylamino, C<sub>1</sub>-C<sub>18</sub> alkylaminocarbonyl, C<sub>2</sub>-C<sub>36</sub> dialkylaminocarbonyl, C<sub>1</sub>-C<sub>18</sub> alkyloxycarbonyl, C<sub>7</sub>-C<sub>18</sub> arylcarboxamido, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl or aryl portions of said R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> are optionally substituted one or more times by substituents selected from the group consisting of F, Cl, Br, I, hydroxy, carboxylic acid, a carboxylic acid ester of a C<sub>1</sub>-C<sub>6</sub> alcohol, sulfonic acid, amino, C<sub>1</sub>-C<sub>6</sub> alkylamino, C<sub>2</sub>-C<sub>6</sub> dialkylamino and C<sub>1</sub>-C<sub>6</sub> alkoxy; or a pair of adjacent R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> substituents when taken in combination, form a fused 6-membered aromatic ring that is optionally further substituted by carboxylic acid; and

wherein L is a covalent linkage;

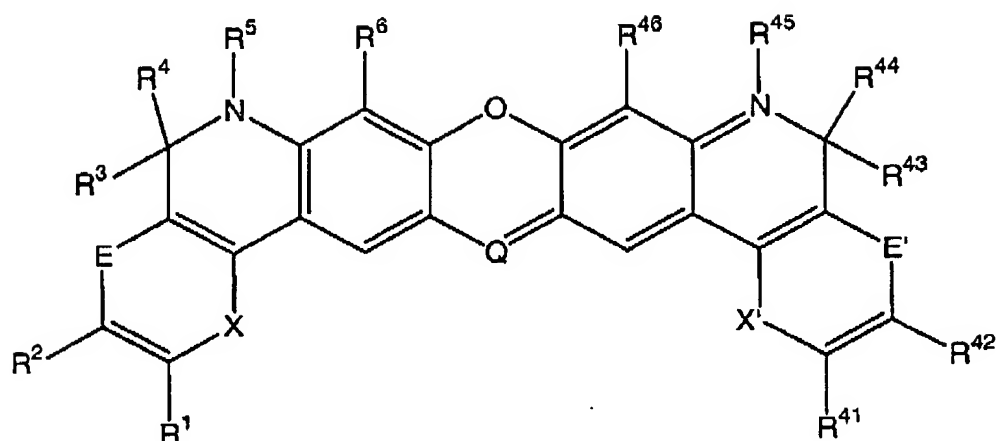
R<sub>x</sub> is a reactive group; and

S<sub>C</sub> is a conjugated substance.

22. (Original) A compound having a formula:



Diwu *et al.*  
Serial No. 10/713,670



wherein  $R^1$ ,  $R^2$ ,  $R^6$ ,  $R^{41}$ ,  $R^{42}$ , and  $R^{46}$  are independently selected from the group consisting of hydrogen, cyano, halogen, carboxylic acid, sulfonic acid,  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_C$ , wherein said alkyl or alkoxy is optionally substituted by carboxylic acid, sulfonic acid, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, azido, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^1$  in combination with  $R^2$ , or  $R^{41}$  in combination with  $R^{42}$ , or both, forms a fused aromatic or heteroaromatic ring that is optionally sulfonated one or more times, or said ring is substituted by  $-L-R_x$  or  $-L-S_C$ ;

$R^3$ ,  $R^4$ ,  $R^{43}$ , and  $R^{44}$  are independently selected from the group consisting of hydrogen,  $C_1$ - $C_6$  alkyl, an aromatic or heteroaromatic ring,  $-L-R_x$  and  $-L-S_C$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, hydroxy, or halogen and said aromatic or heteroaromatic ring is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  alkoxy,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^2$  in combination with  $R^3$ , or  $R^{42}$  in combination with  $R^{43}$ , or  $R^3$  in combination with  $R^4$ , or  $R^{43}$  in combination with  $R^{44}$ , or any combination thereof, forms a 5- or 6-membered alicyclic ring;

Diwu *et al.*  
Serial No. 10/713,670

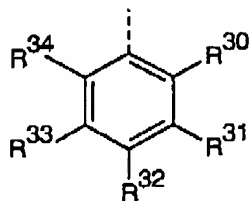
$R^5$  and  $R^{45}$  are independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2$ - $C_6$  alkyl, aryl, heteroaryl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen and said aryl or heteroaryl is optionally substituted one or more times by  $C_1$ - $C_6$  alkyl,  $C_1$ - $C_6$  perfluoroalkyl, cyano, halogen, carboxylic acid, sulfonic acid, or halomethyl;

or  $R^4$  in combination with  $R^5$ , or  $R^5$  in combination with  $R^6$ , or  $R^{44}$  in combination with  $R^{45}$ , or  $R^{45}$  in combination with  $R^{46}$ , or any combination thereof, forms a 5- or 6-membered allcyclic ring;

wherein one of said E, E', X' and X is O, S, or  $NR^8$ , provided that E and X or E' and X' are not both present;

wherein  $R^5$  is independently selected from the group consisting of hydrogen, methyl, carboxymethyl,  $C_2$ - $C_6$  alkyl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; and

Q is N or  $CR^{28}$ , wherein  $R^{28}$  is independently selected from the group consisting of hydrogen, F, CN, carboxylic acid, a carboxylic acid ester of a  $C_1$ - $C_6$  alcohol, a  $C_1$ - $C_6$  alkyl,  $-L-R_x$  and  $-L-S_c$ , wherein said alkyl is optionally substituted by carboxylic acid, sulfonic acid, amino, or halogen; or  $R^{28}$  comprises a formula



wherein  $R^{30}$ ,  $R^{31}$ ,  $R^{32}$ ,  $R^{33}$  and  $R^{34}$  are independently selected from the group consisting of hydrogen, F, Cl, Br, I, sulfonic acid, carboxylic acid, CN, nitro, hydroxy, azido, amino, hydrazino,  $C_1$ - $C_{18}$  alkyl,  $C_1$ - $C_{18}$  alkoxy,  $C_1$ - $C_{18}$  alkylthio,  $C_1$ - $C_{18}$  alkanoylamino,  $C_1$ - $C_{18}$

Diwu *et al.*

Serial No. 10/713,670

alkylaminocarbonyl, C<sub>2</sub>-C<sub>36</sub> dialkylaminocarbonyl, C<sub>1</sub>-C<sub>18</sub> alkyloxycarbonyl, C<sub>7</sub>-C<sub>18</sub> arylcarboxamido, -L-R<sub>x</sub> and -L-S<sub>C</sub>, wherein said alkyl or aryl portions of said R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> are optionally substituted one or more times by substituents selected from the group consisting of F, Cl, Br, I, hydroxy, carboxylic acid, a carboxylic acid ester of a C<sub>1</sub>-C<sub>6</sub> alcohol, sulfonic acid, amino, C<sub>1</sub>-C<sub>6</sub> alkylamino, C<sub>2</sub>-C<sub>6</sub> dialkylamino and C<sub>1</sub>-C<sub>6</sub> alkoxy; or a pair of adjacent R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup> and R<sup>34</sup> substituents when taken in combination, form a fused 6-membered aromatic ring that is optionally further substituted by carboxylic acid; and

wherein L is a covalent linkage;

R<sub>x</sub> is a reactive group; and

S<sub>C</sub> is a conjugated substance;

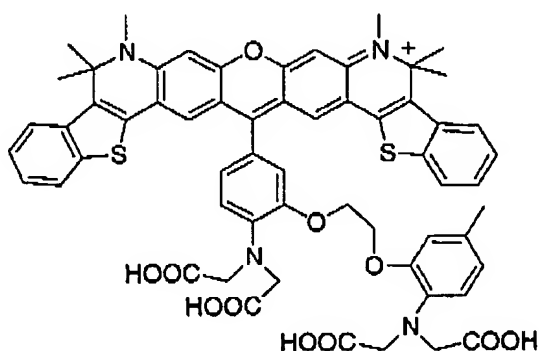
with the proviso that at least one of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>8</sup>, R<sup>28</sup>, R<sup>30</sup>, R<sup>31</sup>, R<sup>32</sup>, R<sup>33</sup>, R<sup>34</sup>, R<sup>41</sup>, R<sup>42</sup>, R<sup>43</sup>, R<sup>44</sup>, R<sup>45</sup> and R<sup>46</sup> is a conjugated substance.

23. (Original) The compound according to Claim 22, wherein E and E' are each S; R<sup>1</sup> in combination with R<sup>2</sup> form a aromatic ring and R<sup>41</sup> in combination with R<sup>42</sup> form an aomatic ring.
24. (Original) The compound according to Claim 23, wherein said conjugated substance is independently selected from the group consisting of an amino acid, a peptide, a protein, a tyramine, a carbohydrate, a metal chelating moiety, a nucleoside, a nucleotide, an oligonucleotide, a nucleic acid, a hapten, a psoralen, a drug, a hormone, a lipid, a lipid assembly, a polymer, a polymeric microparticle, a biological cell, and a virus.
25. (Original) The compound according to Claim 24, wherein said conjugated substance is a metal chelating moiety wherein said metal chelating moiety is optionally substituted by a reactive group.

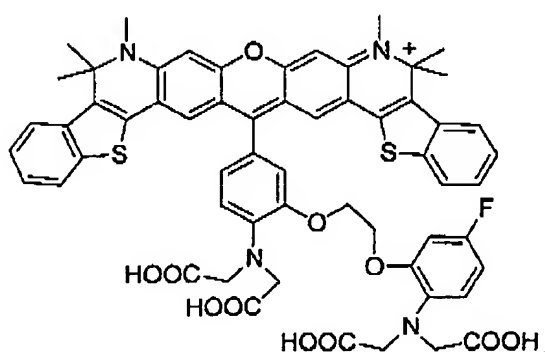
Diwu *et al.*

Serial No. 10/713,670

26. (Original) The compound according to Claim 25, wherein said metal chelating moiety is BAPTA.
27. (Original) The compound according to Claim 26, wherein said  $R^{28}$  is said BAPTA.
28. (Original) The compound according to Claim 27, wherein said reactive group is selected from the group consisting of a carboxylic acid, a succinimidyl ester of a carboxylic acid, a maleimide, a cadaverine, a benzophenone, an aryl azide and a diazine.
29. (Original) The compound according to Claim 27, wherein said compound is according to formula



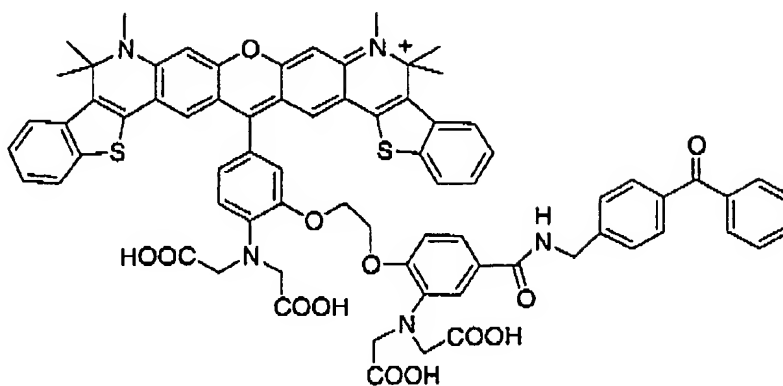
or



30. (Original) The compound according to Claim 28, wherein said compound is according to formula

Diwu *et al.*

Serial No. 10/713,670



Diwu *et al.*  
Serial No. 10/713,670

**CONCLUSION**

In view of the above amendments and remarks, It is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned at (541) 335-0203.

Respectfully submitted,

Date: January 27, 2006

Koren J. Anderson  
Koren J. Anderson, Ph.D.  
Reg. No. 51,061

Molecular Probes, Inc.  
29851 Willow Creek Rd.  
Eugene, Oregon, 97402  
Phone: (541) 335-0203  
Facsimile: (541) 335-0188